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(54) Title: PROAPOPTOTIC PEPTIDES, DEPENDENCE POLYPEPTIDES AND METHODS OF USE

(57) Abstract

The present invention provides substantially pure proapoptotic dependence peptides. The peptides consist substantially of the sequence of an active dependence domain selected from the group of dependence polypeptides consisting of $p75^{NTR}$, androgen receptor, DCC, huntingtin polypeptide, Machado–Joseph disease gene product, SCA1, SCA2, SCA6 and atrophin–1 polypeptide. Substantially pure proapoptotic dependence peptides include SATLDALLAALRRI (SEQ ID NO:3), Q14 (SEQ ID NO:7), SATLDALLAALGGI (SEQ ID NO:4), SATLDALLAALRGI (SEQ ID NO:5), SATLQALLAALRRI (SEQ ID NO:6), tat–GG–SATLDALLAALRRI (SEQ ID NO:37) and tat–GG–Q14 (SEQ ID NO:36). The invention also provides a method of increasing cell survival. The method consists of inhibiting the function of an active proapoptotic dependence domain. A method of increasing cell survival consisting of preventing or reducing the rate of formation of an active proapoptotic dependence domain is also provided. The invention further provides a method of identifying compounds which prevent or inhibit apoptosis. The method consists essentially of administering a test compound to a cell undergoing dependence domain mediated apoptosis, and determining whether the compound increases cell survival. A method of reducing the severity of a proapoptotic dependence domain mediated pathological condition is also provided. The method consists of inhibiting the function of an active dependence domain. Additionally provided is a method of reducing the severity of a pathological condition mediated by unregulated cell growth. The method consists of cytoplasmically administering a proapoptotic dependence peptide.